REMARKS/ARGUMENTS

The claims are 2-4 and 7-21. Claim 8 has been amended to place it in independent form as a method for preparing a pharmaceutical composition and claims 2-4, 10 and 16-19 have been amended to improve their form. Reconsideration is expressly requested.

In the Office Action, the Examiner pointed out that the claims 8-10 were improperly dependent from a method of use claim as the body of the claims themselves were drawn to the method of making the solid lipidic nanoparticles and were treated by the Examiner as methods of making. In response, Applicants have amended claim 8 to place it in independent form as a method for preparing a pharmaceutical composition, which it is respectfully submitted overcomes the Examiner's objection on the basis of this informality.

As stated above, Applicants elect Group I, claims 2-4, 7 and 11-13, and triamcinolone as the species with claims 2-4, 7 and 11-13 readable on the species, and claim 11 being generic, for

further prosecution and respectfully traverse the requirement for restriction for the following reasons:

As an initial matter, it is respectfully submitted that the Examiner's premise for requiring restriction is incorrect as the *Anselem et al. U.S. Patent No. 5,662,932* does not anticipate the claims and in fact the nanoemulsions with which *Anselem et al. et al.* is concerned have nothing to do with the SLN which characterize Applicants' invention as recited in the claims.

The solid lipid nanoparticles (SLN) of Applicants' claims are produced from a microemulsion in hot water of lipids, where the nanodroplets have a diameter of about 100nm and form a quite limpid system. This microemulsion is poured into cold water where the nanoparticles form, giving in any case a limpid system, where the nanoparticles have the same diameter of the starting nanoparticles.

Anselem et al. prepares their nanoemulsions by dissolving the phospholipids or other lipids together with the drug in

dichloromethane, then evaporating the solvent to dryness and adding water to the dry rest, under homogenization conditions. In some cases, the emulsion is filtered with a filter of 0.2 micron.

Accordingly, it is respectfully submitted that *Anselem et al.* is not speaking of the same product to which Applicants' claims are concerned and therefore cannot be considered to anticipate Applicants' claims, which was the basis for the Examiner's objection to the lack of unity for purposes of imposing the restriction requirement. Also from the point of view of administration, the two products are different, because *Anselem et al.* puts directly in the eyes their nanoemulsions containing the drug, while Applicants disperse in water the SLN containing the drug and apply to the eyes the obtained aqueous dispersion.

It is respectfully submitted, moreover, that the Examiner's requirement for selection of a single species is inappropriate in this case to the extent that it requires Applicants to select a

a single active substance for the reasons set forth in Applicants' previous Response to Restriction Requirement filed May 30, 2008.

In addition, it is believed that any search for the method for the treatment of ophthalmic diseases embodied in Group I, claims 2-4, 7 and 11-13, would necessarily include a search for the compositions as defined in Group II, claims 14-21, and the method of preparing a pharmaceutical composition containing solid lipidic nanoparticles as defined in Group III, claims 8-10. Also, it is believed that any search for the triamcinolone species would necessarily include a search for the pharmacological active substances embodied in the remaining species. Thus, the simultaneous search for all the groups and species is believed not to constitute an unreasonable search for the Patent Examiner.

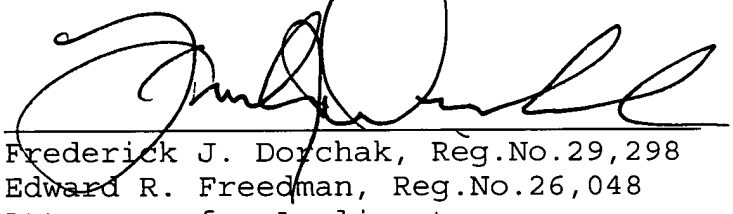
In addition, it is believed that the objectives of streamlined examination and compact prosecution would be promoted if a search were conducted simultaneously for all the groups and

species. Also, the necessity of filing multiple patent applications in this case does not serve to promote the public interest because of the extra expense that is involved, in filing fees and examination costs, as well as the burden upon the public, due to the necessity of searching through a multiplicity of patent files in order to find the complete range of the subject matter claimed in several different patents that could otherwise be found in one issued patent only.

Applicants reserve the right to file divisional applications for the non-elected groups and species.

In summary, claims 2-4, 8, 10 and 16-19 have been amended and an election with traverse of Group I, claims 2-4, 7 and 11-13 and species triamcinolone has been made. For all these reasons, it is respectfully requested that the restriction requirement under 35 U.S.C. 121 be withdrawn and that an action on the merits of all the claims be rendered.

Respectfully submitted,
Maria Rosa GASCO ET AL



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Enclosure: Copy of Merck Index for triamcinolone (page 1511)

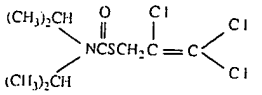
I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on October 30, 2008.

Amy Klein

Amy Klein

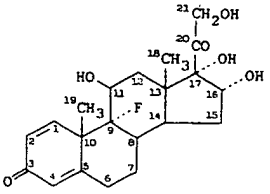
Yellow crystals from dimethylformamide + water or acetic acid, mp 280°.

9510. Triallate. *Bis(1-methylethyl)carbamothioic acid S-(2,3,3-trichloro-2-propenyl) ester; diisopropylthiocarbamic acid S-(2,3,3-trichloroallyl) ester;* 2,3,3-trichloro-2-propene-1-thiol diisopropylcarbamate; *S*-2,3,3-trichloroallyl diisopropylthiocarbamate; *S*-(2,3,3-trichloro-2-propenyl) bis(1-methylethyl)carbamothioate; CP 23426; Avadex BW; Far-Go. $C_{10}H_{16}Cl_3NOS$; mol wt 304.66. C 39.42%, H 5.29%, Cl 34.91%, N 4.60%, O 5.25%, S 10.52%. Prepn: M. W. Harman, J. J. D'Amico, U.S. pat. **3,330,821** (1967 to Monsanto). Herbicidal activity: R. Grover *et al., Weed Res.* **19**, 363 (1979). Mutagenic evaluation *in vitro* (Ames Test): F. De Lorenzo *et al., Cancer Res.* **38**, 13 (1978); G. R. Douglas *et al., Mutat. Res.* **85**, 45 (1981). Soil persistence: A. E. Smith, B. J. Hayden, *Bull. Environm. Contam. Toxicol.* **29**, 240 (1982). Field studies for pre-emergent use: T. G. Reeves, C. L. Touhey, *Aust. J. Exp. Agr. Anim. Husb.* **12**, 55 (1972); E. M. Randall, R. H. Jarvis, *Exp. Husb.* **38**, 32 (1982); post-emergent use: R. P. Garnett, *Aspects Appl. Biol.* **13**, 73 (1980). GC determn in soils: A. E. Smith, *J. Chromatog.* **97**, 103 (1974). HPLC determn in soils: A. Pena Heras, F. Sanchez-Rasero, *ibid.* **358**, 302 (1986).



USE: Herbicide.

9511. Triamcinolone. *9-Fluoro-11,16,17,21-tetrahydroxypregna-1,4-diene-3,20-dione;* Δ^1-9α-fluoro-16α-hydroxyhydrocortisone; 9α-fluoro-16α-hydroxyprednisolone; Δ^1-16α-hydroxy-9α-fluorohydrocortisone; 16α-hydroxy-9α-fluoroprednisolone; CL 19823; Adcortyl; Aristocort; Celeste; Cinolone; Delphicort; Extracort; Kenacort; Ledercort; Omcilon; Orion; Triamcet; Tricortale; Volon. $C_{21}H_{27}FO_6$; mol wt 394.45. C 63.94%, H 6.90%, F 4.82%, O 24.34%. Prepn: Bernstein *et al., J. Am. Chem. Soc.* **78**, 5693 (1956); **81**, 1689 (1959); Thoma *et al., ibid.* **79**, 4818 (1957); Bernstein *et al.*, Allen *et al.*, U.S. pats. **2,789,118**; **3,021,347** (1957, 1962, both to Am. Cyanamid). Comprehensive description: K. Florey, Ed. in *Analytical Profiles of Drug Substances* **vol. 1** (Academic Press, New York, 1972) pp 367-396, 423-442; D. H. Sieh, *ibid.* **vol. 11**(1982) pp 593-614, 651-661.



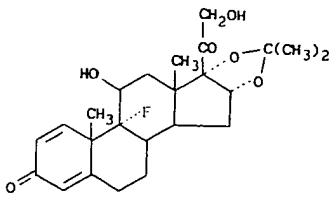
Crystals, mp 269-271°. mp also reported as 260-262.5°. $[\alpha]_D^{25}$ +75° (acetone). uv max: 238 nm (ε 15800).

16α,21-Diacetate, $C_{25}H_{31}FO_8$, *16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-1,4-pregnadiene-3,20-dione, Polcortolon; CINO-40, Cenocort, Tracilon, Triamcin.* Solvated crystals, mp 186-188° (with effervescence, mp 235° after drying). $[\alpha]_D^{25}$ +22° (chloroform). uv max: 239 nm (ε 15200).

THERAP CAT: Glucocorticoid.

THERAP CAT (VET): Adrenocortical steroid. Anti-inflammatory glucocorticoid.

9512. Triamcinolone Acetonide. *9-Fluoro-11,21-dihydroxy-16,17-[1-methylethylidenebis(oxy)]pregna-1,4-diene-3,20-dione; 9α-fluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with acetone;* 9α-fluoro-16α-hydroxyprednisolone acetonide; triamcinolone 16α,17-acetonide; 9α-fluoro-11β,21-dihydroxy-16α,17α-isopropylidenedioxy-1,4-pregnadiene-3,20-dione; 9α-fluoro-16α,17-isopropylidenedioxyprednisolone; Adcortyl-A; Aristoderm; Cutinolone Simple; Flutex; Ftorocort; Kenacort-A; Kenalog; Kenaquart; Ledercort D; Omcilon-A; Respicort; Rineton; Solodelf; Tramacin; Tricinolon; Vetalog; Volon A; Volonimat. $C_{24}H_{31}FO_6$; mol wt 434.49. C 66.34%, H 7.19%, F 4.37%, O 22.09%. Prepd by stirring a suspension of triamcinolone in acetone in the presence of a trace of perchloric acid: Fried *et al., J. Am. Chem. Soc.* **80**, 2338 (1958); Bernstein *et al., ibid.* **81**, 1689 (1959); Bernstein, Allen, U.S. pat. **2,990,401** (1961 to Am. Cyanamid). Alternate synthesis using 2,3-dibromo-5,6-dicyanoquinone: Hydorn, U.S. pat. **3,035,050** (1962 to Olin Mathieson). Clinical trial in chronic asthma: I. L. Bernstein *et al., Chest* **81**, 20 (1982). Comprehensive description: K. Florey, Ed. in *Analytical Profiles of Drug Substances* **vol. 1** (Academic Press, New York, 1972) pp 397-421; D. H. Sieh, *ibid.* **vol. 11** (1982) pp 615-649.



Crystals, mp 292-294°. $[\alpha]_D^{23}$ +109° (c = 0.75 in chloroform). uv max (abs alc.): 238 nm (ε 14,600). Sparingly sol in methanol, acetone, ethyl acetate.

21-Acetate, crystals, mp 268-270°. $[\alpha]_D^{23}$ +92° (c = 0.59 in chloroform).

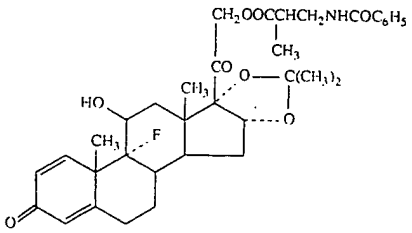
21-Disodium phosphate, $C_{24}H_{30}FNa_2O_9P$, *Aristosol.*

21-Hemisuccinate, $C_{28}H_{35}FO_9$, *Solutedarol.*

THERAP CAT: Glucocorticoid; anti-inflammatory; antiasthmatic (inhalant).

THERAP CAT (VET): Glucocorticoid, anti-inflammatory.

9513. Triamcinolone Benetonide. *(11β,16α)-21-[3-(Benzoylamino)-2-methyl-1-oxopropoxy]-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione; 9-fluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with acetone 21-ester with N-benzoyl-2-methyl-β-alanine;* 9α-fluoro-16α-hydroxyprednisolone 16α,17α-acetonide 21-(β-benzoylamino)-isobutyrate; triamcinolone acetonide β-benzoylaminoisobutyrate; TBI; Tibicorten. $C_{35}H_{42}FNO_8$; mol wt 623.73. C 67.40%, H 6.79%, F 3.05%, N 2.24%, O 20.52%. Prepn: C. Cavazza *et al.*, Ger. pat. **2,047,218**; *eidem*, U.S. pat. **3,749,712** (1971, 1973 both to Sigma-Tau). Pharmacology: E. T. Ordonez, *Arzneimittel-Forsch.* **21**, 248 (1971). Percutaneous absorption by rats and rabbits: W. H. Down *et al., Toxicol. Letters* **1**, 95 (1977). Clinical study: D. J. Tazelaar, *J. Int. Med. Res.* **5**, 338 (1977). HPLC analysis: S. Muck *et al., Boll. Chim. Farm.* **120**, 240 (1981).



Crystalline powder, mp 203-207°. $[\alpha]_D^{20}$ +96° ±3° (c = 1 in ethanol). Sol in methanol, acetone, ethanol, dioxane, pyridine, DMF, chloroform. Insol in water.

THERAP CAT: Glucocorticoid; topical anti-inflammatory.

9514. Triamcinolone Hexacetonide. *21-(3,3-dimethyl-1-oxobutoxy)-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione; 9-fluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with acetone, 21-(3,3-dimethylbutyrate);* 21-tert-butylacetate-9α-fluoro-11β-hydroxy-16α,17α-(isopropylidenedioxy)pregna-1,4-diene-3,20-dione; 21-(3,3-dimethylbu-